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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/564,273

07/31/2007

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EXAMINER

BETTON, TIMOTHY E

ART UNIT

PAPER NUMBER

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/564,273	Applicant(s) VAISMAN, JAKOV	
	Examiner TIMOTHY E. BETTON	Art Unit 1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 August 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 62,63,66,69-76,78-80,82 and 83 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 62,63,66,69-76,78,79, 80,82 and 83 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6 August 2010 has been entered.

Response to Arguments

Applicants' remarks filed on 6 August 2010 have been acknowledged and duly made of record.

Likewise, applicants' amendments to claims 76, 78, 80, and 83 have been acknowledged and duly made of record.

Rejections under 35 U.S.C. §112, second paragraphs are traversed by applicants' in view of applicants' amendments officially made of record 6 August 2010.

Applicants' arguments are considered and are found persuasive in this instance.

The Rejection under 35 U.S.C. §102(b) as allegedly anticipated by Altabet is traversed by applicants' as allegedly failing to teach a combination of two or more routes of administration that act synergistically.

Specifically, the sole Altabet reference is alleged by applicants' to be insufficient to establish anticipation due to the express disclosure of a first formulation comprising an

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antidepressant formulated for nasal administration; and a second formulation comprising an antidepressant formulated for local administration to at least part of the male genitalia. Neither the Office Action nor the Advisory Action even alleges that Altabet discloses any such combination. Applicants' respectfully submit that Altabet does not disclose each and every element of the present claims, and therefore does not and cannot anticipate the pending claims.

Applicants' arguments are considered and are found persuasive in as far as Altabet does not expressly teach a first formulation comprising an antidepressant formulated for nasal administration; and a second formulation comprising an antidepressant formulated for local administration to at least part of the male genitalia.

Further, applicants' argue that the rejection under 35 U.S.C. §103(a) is allegedly improper for providing no teaching, suggestion, or motivation to combine the references

In response to applicant's argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, Bar-Or is reiterated for clarity:

Bar-Or teaches that formulations were known in the prior art using anti-depressants, and that choosing which one to use would be driven by effective response in a given patient. The

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combination of any known effective antidepressants would have been obvious in view of Kerkhoven (especially since it may require determining specific combinations that are effective in a given patient. This would have been obvious to the skilled artisan. Further, it is asserted that the claims that are drawn to the administration directly to the genitalia for specific time periods to be obvious in view of the teachings of transdermal delivery of the medicaments taught in the prior art. These limitations (application to the genitalia for specific time periods) are not deemed to provide a distinction over the teachings of the prior art for transdermal delivery. Simultaneous delivery via two different methods would have been obvious, as it was known in the art that delivery through the skin versus the mucous membrane of the nose would deliver different effective amounts of the medicament. Nasal delivery will provide for a faster delivery to the bloodstream, while a transdermal delivery can provide a slower, sustained release of the medicament through the skin as an advantage for patients also requiring a steady dose of medicament over a longer period of time following the initial burst of drug. In this regard, applicant points to the opinion evidence in the specification at pages 14 and 15.

Bodor specifically teach that these embodiments of formulations drawn to the composition is designed for **nasal, vaginal**, or rectal administration, i.e. a nonoral or noninjectable route of administration is used Please see column 5 (underneath remainder of table beginning with Tuttle (incorporated by reference).

The reference to '*vaginal*' above is interchangeable with the penile reference in the claimed invention in as far and only in as far as Bodor contemplates and teaches administration to the genitalia and does not expressly preclude administration to the male genitalia.

Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of the Claims

Claims 62-63, 66, 69-76, 78,79,80, and 82-83 are pending further prosecution on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 62-63, 66, and 69-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bar-Or (USPGPUB 2002/0132857 A1) in view of Crenshaw et al. (USPN 5151448) and Rojas-Corrales et al. [Journal of Psychopharmacology 18(3):404-411 (2004)] and Shargel et al. (Applied Biopharmaceutics and Pharmacokinetics, 4th ed. Appleton and Lange, Stamford, CT pp108-109, pp 154-163).

Bar-Or teaches that formulations were known in the prior art using anti-depressants, and that choosing which one to use would be driven by effective response in a given patient. The combination of any known effective antidepressants would have been obvious in view of Kerkhoven (especially since it may require determining specific combinations that are effective in a given patient. This would have been obvious to the skilled artisan. Further, it is asserted that the claims that are drawn to the administration directly to the genitalia for specific time periods to be obvious in view of the teachings of transdermal delivery of the medicaments taught in the prior art. These limitations (application to the genitalia for specific time periods) are not deemed to provide a distinction over the teachings of the prior art for transdermal delivery. Simultaneous deliver via two different methods would have been obvious, as it was known in the art that

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delivery through the skin versus the mucous membrane of the nose would deliver different effective amounts of the medicament. Nasal delivery will provide for a faster delivery to the bloodstream, while a transdermal delivery can provide a slower, sustained release of the medicament through the skin as an advantage for patients also requiring a steady dose of medicament over a longer period of time following the initial burst of drug. In this regard, applicant points to the opinion evidence in the specification at pages 14 and 15.

Bar-Or reference teaches Tramadol. Bar-Or paragraphs 4-7 in the context of treatment of premature ejaculation using anti-depressants, teaches that although Bar-Or seems to suggest problems with the use of antidepressants for treating premature ejaculation, this caution is only that the particular antidepressants of the prior art may not be effective for all patients. See paragraph 5, lines 6-7. Tramadol is suggested as a new treatment option. In fact, Tramadol is inherently also an antidepressant.

Bar-Or also teach that this composition may be optimized to be given topically (see paragraph 20 at line 4).

The following is cited only as evidence of inherency of the prior art product. See the abstract by Rojas-Corrales et al. [Journal of Psychopharmacology 18(3):404-411 (2004)] wherein it is demonstrated that Tramadol “has an effect comparable to clinically effective antidepressants in a test predictive of antidepressant activity, without behavioural implications [and] has an inherent antidepressant-like (mood-improving) activity. Therefore the prior art of Bar-Or teaches that the prior art recognized many alternatives to treating premature ejaculation using antidepressants. Tramadol is one of those alternatives that may be selected based on what is effective in a given patient.

However, Crenshaw et al. teach an exact dosage of fluoxetine which is explicitly indicated for male human patient premature ejaculation (see abstract).

Accordingly, the specific dosages as disclosed for fluoxetine, a well-established antidepressant, are about 5 milligrams to about 80 milligrams for a time period of at least about 3 months, and preferably for time period of at least about 6 months.[...]. A daily dose of about 20 milligrams is preferred (column 3, lines 10-18). Exemplifications of the variability in dosing are further elucidated in the rest of column 3 of the instant specification.

Crenshaw et al. teach [that] [f]or the treatment contemplated by the present invention, [...], other routes of administration [teach that], e.g., **parenteral**, by suppositories, buccal dosage forms, *skin patch, and the like, can also be utilized*. (col. 2 lines 64-68). Thus the skin patch constitutes a transdermal dressing which therefore also constitutes a local administration to at least a part of the male genitalia. The limitation drawn to “*and the like*” constitutes any extrapolation reasonably conceived by the one of skill in view of the scope and content of the invention.

Crenshaw does not expressly teach the limitations of claims 70-74. However, in this instance, applicants' attention are directed to obviousness in combining active agents which exemplify the same resulting effect on a disease, disorder, and/or condition such as premature ejaculation. In the instance of the alleged invention, it would be obvious to combine an SSRI with a newer antidepressant on the market such as MAOI to achieve greater therapeutic efficacy.

Shargel et al. teach in the first full paragraph on page 1 of 14 parenteral administration as also disclosed *supra* by Crenshaw et al. as also being inclusive of nasal (which constitutes topical

administration to the mucous membrane) and topical/local administration: (What is Shargel doing in this rejection? Shouldn't this be in your prior rejection? Please clarify.)

One method of classifying routes of administration is ENTERAL and PARENTERAL. Enteral means to do with the GI tract and includes oral, buccal, and rectal. Parenteral means not through the alimentary canal and commonly refers to injections such as IV, IM, and SC; but could also include topical and inhalation. We can also distinguish IV from the rest, as with all others at least one membrane must be crossed, thus an absorption process is involved in the administration and the pharmacokinetic model.

Thus, by virtue of nasal and topical administration being classified under the same general mode of administration, i.e., *parenteral*, the one of ordinary skill in the pertinent art would reasonably conclude that the administration of a composition indicated for the same purpose but administered via different routes would be reasonably expected to achieve additive and/or synergistic results. The propensity for the one of skill to combine two types of distinct modes under the same general classification is reasonably obvious in order to achieve a probable additive and/or synergistic effect.

Claims 78, 79, 80, 82, and 83 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bar-Or (USPGPUB 2002/0132857 A1) in view of Crenshaw et al. (USPN 5151448) and in further view of Rojas et al. as applied to claims 62-63, 66, 69-76 above and further in view of Bodor et al (USPN 5024998).

Bar-Or in view of Crenshaw and/or Rojas et al. do not teach a medicament comprising of a serotonin reuptake inhibitor and MAO-inhibitors. They also do not teach the claimed enhancers such as cyclodextrin.

Bodor et al teach that the **cyclodextrin complexes** of the invention are preferably administered in the form of a pharmaceutical composition comprising the selected complex and a nontoxic pharmaceutically acceptable carrier therefor. Suitable nontoxic pharmaceutically acceptable carriers for use with the topic complexes, e.g., those less toxic than the target drug species themselves, will be apparent to those skilled in this art. [...] Obviously, the choice of suitable carriers will depend upon the route of administration and the exact nature of the particular dosage form selected, as well as upon the identity of the active drug species, the redox derivative and the complex to be administered. Contemplated routes of administration for the complexes of the invention include oral, buccal, sublingual, topical (including ophthalmic), rectal, **vaginal**, **nasal**, and parenteral (including intravenous, intramuscular and subcutaneous).

In column 7 at lines 43-49, Bodor teaches aqueous media by which the active agents may be dissolved

Further, Bodor teaches antidepressants in column 18 at line 58 and in column 23 at lines 49 and 59-60, respectively.

Bodor specifically teach that these embodiments of formulations drawn to the composition is designed for **nasal**, **vaginal**, or rectal administration, i.e. a nonoral or noninjectable route of administration is used Please see column 5 (underneath remainder of table beginning with Tuttle (incorporated by reference).

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The reference to '*vaginal*' above is interchangeable with the penile reference in the claimed invention in as far and only in as far as Bodor contemplates and teaches administration to the genitalia and does not expressly preclude administration to the male genitalia.

Further, in column 23 at lines 24 and 25, Bodor teaches MAO inhibitors.

Accordingly, Bodor teaches fluoxetine, a well-established and art-known serotonin reuptake inhibitor in column 24 at line 22.

MPEP cites:

2144.06 [R-6] Art Recognized Equivalence for the Same Purpose

I. COMBINING EQUIVALENTS KNOWN FOR THE SAME PURPOSE

“It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art.” *In re Kerkhoven.*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980)

As for the limitations drawn to via the combination of nasal and local administration, the contemplation to optimize therapy is reasonably identified via the disclosure of Bar-Or with Bodor providing additional motivation based upon the nature of the formulations comprising cyclodextrin (HPBCD), *supra*. Based upon the nature of the art, it would have been apparent and *prima facie* obvious to the one of skill to optimize the characterization of such therapy to achieve satisfaction and/or claimed the desired effect.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY E. BETTON whose telephone number is (571)272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TEB

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627

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